

**AMENDMENTS TO THE CLAIMS**

This listing of claims will replace all prior versions and listings of claims in the application:

**Listing of Claims:**

1.-20. **(Canceled)**

21. **(Previously presented)** A vector comprising:

- (1) a nucleic acid encoding a chimeric nuclease that comprises: (i) a DNA binding domain; (ii) a cleavage domain; and (iii) a nuclear localization signal; and
- (2) a nucleic acid comprising a repair substrate that comprises: (i) a nucleic acid sequence that is substantially identical to a region flanking a target sequence in chromosomal DNA; and (ii) a nucleic acid sequence which replaces the target sequence upon recombination between the repair substrate and the target sequence.

22-27. **(Canceled)**

28. **(Previously presented)** A mammalian cell comprising: (a) a chimeric nuclease; and (b) a repair substrate, wherein the chimeric nuclease comprises:

- (i) a nuclear localization signal;
- (ii) a DNA binding domain; and
- (iii) a cleavage domain,

and wherein the repair substrate comprises:

- (i) a nucleic acid sequence that is substantially identical to a region flanking a target sequence in chromosomal DNA; and
- (ii) a nucleic acid sequence which replaces the target sequence upon recombination between the repair substrate and the target sequence.

29-39. **(Canceled)**

40. **(Previously presented)** A mammalian cell comprising a nucleic acid encoding a chimeric nuclease and a nucleic acid comprising a repair substrate, wherein the chimeric nuclease comprises:

- (i) a nuclear localization signal;

- (ii) a DNA binding domain; and
  - (iii) a cleavage domain,
- and wherein the repair substrate comprises:
- (i) a nucleic acid sequence that is substantially identical to a region flanking a target sequence in chromosomal DNA; and
  - (ii) a nucleic acid sequence which replaces the target sequence upon recombination between the repair substrate and the target sequence.

41-42. **(Canceled)**

43. **(Previously presented)** A method of changing a target sequence in genomic DNA of a mammalian cell, comprising:
- (a) introducing a chimeric nuclease, or nucleic acid encoding the chimeric nuclease, into the cell, wherein said chimeric nuclease comprises: (i) a DNA binding domain; (ii) a cleavage domain; and (iii) a nuclear localization signal; and
  - (b) introducing a repair substrate into the cell, wherein said repair substrate comprises: (i) a nucleic acid sequence that is substantially identical to a region surrounding the target sequence; and (ii) a nucleic acid sequence which changes the target sequence upon recombination between the repair substrate and the target sequence,
- whereby the target sequence is changed by the repair substrate upon recombination.

44.-98. **(Canceled)**

99. **(Previously presented)** The vector of claim 21, wherein the nucleic acid encoding the chimeric nuclease is operably linked to a promoter.
100. **(Previously presented)** The vector of claim 99, wherein the promoter is an inducible promoter.
101. **(Previously presented)** The vector of claim 99, wherein the vector is a viral vector.
102. **(Previously presented)** The vector of claim 21, further comprising a nucleic acid encoding a second chimeric nuclease, wherein the second chimeric nuclease forms a heterodimer with said chimeric nuclease.

103. **(Previously presented)** The cell of claim 28, wherein the chimeric nuclease is encoded by a nucleic acid that is operably linked to a promoter in a vector.
104. **(Previously presented)** The cell of claim 103, wherein the promoter is an inducible promoter.
105. **(Canceled)**
106. **(Previously presented)** The cell of claim 28, wherein the DNA binding domain of the chimeric nuclease comprises a zinc finger domain.
107. **(Previously presented)** The cell of claim 28, wherein the cleavage domain comprises a cleavage domain of a type II restriction endonuclease.
108. **(Previously presented)** The cell of claim 107, wherein the cleavage domain comprises a FokI cleavage domain.
109. **(Previously presented)** The method of claim 43, wherein the target sequence contains an allele that contributes to a disease that is repaired by the repair substrate.
110. **(Previously presented)** The method of claim 43, wherein the target sequence is situated in a gene that is attenuated or inactivated by the repair substrate.
111. **(Previously presented)** The method of claim 43, wherein the target sequence is replaced by a heterologous sequence in the repair substrate.
112. **(Previously presented)** The method of claim 111, wherein the heterologous sequence comprises the coding sequence of a transgene.
113. **(Previously presented)** The method of claim 111, wherein the target sequence is selected such that the coding sequence of a transgene is inserted at a transcriptionally active site.
114. **(Previously presented)** The method of claim 43, wherein introducing the chimeric nuclease into the cell comprises introducing a nucleic acid encoding the chimeric nuclease into the cell, whereby the chimeric nuclease is produced in the cell.

- 115. **(Previously presented)** The method of claim 114, wherein the nucleic acid encoding the chimeric nuclease and the repair substrate are present in a single vector introduced into the cell.
- 116. **(Previously presented)** The method of claim 114, wherein the nucleic acid encoding the chimeric nuclease is operably linked to a promoter in a vector.
- 117. **(Previously presented)** The method of claim 116, wherein the promoter is an inducible promoter.
- 118. **(Canceled)**
- 119. **(Previously presented)** The method of claim 43, wherein the DNA binding domain of the chimeric nuclease comprises a zinc finger binding domain.
- 120. **(Previously presented)** The method of claim 43, wherein the cleavage domain comprises a cleavage domain of a restriction endonuclease.
- 121. **(Previously presented)** The method of claim 120, wherein the cleavage domain comprises a FokI cleavage domain.
- 122. **(Previously presented)** The method of claim 43, wherein the chimeric nuclease forms a heterodimer of two different chimeric nucleases.
- 123. **(Previously presented)** The method of claim 43, wherein the target sequence includes an allele that participates in the causation of a disease.
- 124. **(Previously presented)** The method of claim 43, wherein the repair substrate is operably linked to a promoter.
- 125. **(Previously presented)** The method of claim 124, wherein the promoter is an inducible promoter.

126. **(Previously presented)** The method of claim 43, wherein the target sequence is endogenous to the cell.